June 7, 1956

Dr. Herman M. Kalckar
National Institutes of Health
Bethesda 14, Md.

Dear Herman:

Thank you for the latest information in your letter of May 28. It is very interesting that Gal_2^- should have a distinct enzymatic block. How about the other two mutants recently sent you? I hope you will also be able to answer some of my questions about the constitutive character of these enzymes.

This is shaping into a very interesting story, and I am pleased that we will have a chance for a strategy meeting soon. Esther and I are definitely hoping to stay over the weekend at Bethesda, if the NIH will invite us to, and return home on Tuesday after the JH meetings. I don't think we'll have very much chance for a quiet get-together otherwise.

The main question is whether we can correlate the genetic and enzymatic patterns. Would it be easier to characterize the mutants (we have 50-100 more) enzymatically or genetically first? We definitely have to be on the lookout for mutants affecting the other steps in the galactose pathway. Can you think of any shortcuts by which it would be feasible to make a simple, preliminary characterization of the blocks on intact cultures? Are any of the intermediates utilizable for growth by intact Gal+ cells? (E.G. if the galactose-phosphate were it should at least distinguish Gal_2^- from the others).

As to publication, of course I haven't seen any of your detailed experimental results, though the mixture experiment shows pretty clearly that Gal_1^- and Gal_2^- are quite different. I can see no reason why you should not bring up the work at the meeting. I would very seriously question rushing into print at this time. What's the hurry? You can be quite sure that no one else is working on this angle now, and we have a chance to do a rounded analysis on a rationally chosen set of mutants. I would suggest waiting until mutants corresponding to each of the steps have been found (or at least thoroughly looked for); we will then be very interested to determine whether each enzyme corresponds to a single position-effect-group, which is true for the very few examples studied here so far. Meanwhile, we are trying to develop more stocks for your examination. I will be especially interested in Gal_3^- which is in the same position-effect group as Gal_2^- and may be expected to have the same enzymatic block. [illegible]

So far, I do not consider that enough mutants have been studied to support any such generalizations, and I would be quite reticent about publishing such a speculation at the present time (i.e., that position-effect-groups correspond to individual enzymes). This is too important a principle, if it is true, to be casual with the evidence.

Of course, we have many stocks carrying these different mutants, or we would not have given them numbers. What takes time is the task of transferring the Gal$^-$ mutation to a constant genetic background, so that the differences can be ascribed to the Gal mutations, and not other genetic differentials.

Morse, Esther andI have a very extensive paper now in press in GENETICS, entitled "Transductional heterogenotes in Escherichia coli". This gives a detailed account of the genetic interactions of Gal 1,2,4,6 and 7. I am sorry we do not have an extra copy of the ms. on hand at present, but we will bring one with us for us to go over together. You should not bypass Morse as the principal worker on this problem here at Madison; the work here has been an intimate collaboration.

See you soon.

Sincerely,

Joshua Lederberg